

#3
MPG-1 DIV1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Not yet assigned
Group : Not yet assigned
Applicant(s) : Michael Wassenegger et al.
Application No. : Not yet assigned
Confirmation No. : Not yet assigned
Filed : Concurrently herewith
For : NUCLEIC ACID MOLECULES ENCODING
POLYPEPTIDES HAVING THE ENZYMATIC
ACTIVITY OF AN RNA-DIRECTED RNA
POLYMERASE (RdRP)

jc979 U.S. PTO
09/782874
02/08/01

New York, New York
February 8, 2001

Hon. Commissioner for Patents
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), applicants, through their representatives, make of record the following documents in the above-identified application. Copies of all documents were previously submitted in parent application U.S. Application No. 08/811,583. Pursuant to 37 C.F.R. § 1.98(d), applicants have not enclosed copies of the documents herewith. However, applicants stand ready to provide copies at the Examiner's request.*

* For the convenience of the Examiner, applicants have attached duplicate copies of a completed Form PTO-1449 listing these documents.

Express Mail Label
EI187447517US

Articles

David C. Baulcombe, "Mechanisms of Pathogen-Derived Resistance to Viruses in Transgenic Plants", The Plant Cell, Vol. 8, pp. 1833-1844 (October 1996).

David C. Baulcombe, "RNA as a Target and an Initiator of Post-Transcriptional Gene Silencing in Transgenic Plants", Plant Molecular Biology", Vol. 32, pp. 79-88 (1996).

David C. Baulcombe et al., "Ectopic Pairing of Homologous DNA and Post-Transcriptional Gene Silencing in Transgenic Plants", Current Opinion in Biotechnology", Vol. 7, pp. 173-180 (1996).

Frank Boege et al., "In Vitro Transcription of Viroid RNA into Full-Length Copies by RNA-Dependent RNA Polymerase from Healthy Tomato Leaf Tissue", Bioscience Reports, Vol. 2, pp. 185-194 (1982).

Frank Boege, "Simultaneous Presence of Terminal Adenylyl, Cytidylyl, Guanylyl, and Uridylyl Transferase in Healthy Tomato Leaf Tissue: Separation from RNA-Dependent RNA Polymerase and Characterization of the Terminal Transferases", Bioscience Reports, Vol. 2, pp. 379-389 (1982).

Frank Boege et al., "RNA-Dependent RNA Polymerase from Healthy Tomato Leaf Tissue", FEBS Letters, Vol. 121(1), pp. 91-96 (November 1980).

Carlo Cogoni et al., "Conservation of Transgene-Induced Post-Transcriptional Gene Silencing in Plants and Fungi", Trends in Plant Science, Vol. 2(11), pp. 438-443 (November 1997).

William O. Dawson, "Gene Silencing and Virus Resistance: a Common Mechanism", Trends in Plant Science, Vol. 1(4), pp. 107-108 (April 1996).

Ann Depicker et al., "Post-Transcriptional Gene Silencing in Plants", Current Opinion in Cell Biology", Vol. 9, pp. 373-382 (1997).

William G. Dougherty et al., "Transgenes and Gene Suppression: Telling Us Something New?", Current Opinion in Cell Biology, Vol. 7, pp. 399-405 (1995).

C.T. Duda, "Synthesis of Double-Stranded RNA: II. Partial Purification and Characterization of an RNA-Dependent RNA Polymerase in Healthy Tobacco Leaves", Virology, Vol. 92, pp. 180-190 (1979).

C.T. Duda et al., "*In Vitro* Synthesis of Double-Stranded RNA by an Enzyme System Isolated from Tobacco Leaves", Biochim Biophys Acta, Vol. 319(1), pp. 62-71 (August 1973).

Taline Elmayan et al., "Expression of Single Copies of a Strongly Expressed 35S Transgene Can Be Silenced Post-Transcriptionally", The Plant Journal, Vol. 9(6), pp. 787-797 (1996).

James J. English et al., "Requirement of Sense Transcription for Homology-Dependent Virus Resistance and *Trans*-Inactivation", The Plant Journal, Vol. 12(3), pp. 597-603 (1997).

James J. English et al., "Suppression of Virus Accumulation in Transgenic Plants Exhibiting Silencing of Nuclear Genes", The Plant Cell, Vol. 8, pp. 179-188 (February 1996).

D.M.A. Evans et al., "Characterization of RNA-Dependent RNA Polymerases in Healthy and Tobacco Mosaic Virus-Infected Tomato Plants", Annals of Botany, Vol. 54, pp. 271-281 (1984).

R.B. Flavell, "Inactivation of Gene Expression in Plants as a Consequence of Specific Sequence Duplication", Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 3490-3496 (April 1994).

R.B. Flavell et al., "Developmental Regulation of Co-Suppression in *Petunia Hybrida*", Curr. Top. Microbiol. Immunol., Vol. 197, pp. 43-56 (January 1995).

Heinz Fraenkel-Conrat, "RNA-Directed RNA Polymerases of Plants", CRC Critical Reviews in Plant Sciences, Vol. 4(3), pp. 213-226 (1986).

H. Fraenkel-Conrat, "RNA-Dependent RNA Polymerases of Plants", Proc. Natl. Acad. Sci. USA, Vol. 80, pp. 422-424 (January 1983).

Bernd Haas et al., "The Use of Synthetic Oligo-RNA and -DNA as Defined Templates for the Determination of Catalytic Properties of RNA-Directed RNA Polymerase from Tomato Leaf Tissue", Nucleosides & Nucleotides, Vol. 7(5&6), pp. 713-716 (1988).

Masato Ikegami et al., "Characterization of the RNA-Dependent RNA Polymerase of Tobacco Leaves", The Journal of Biological Chemistry, Vol. 254(1), pp. 149-154 (January 1979).

Richard Jorgensen, "Developmental Significance of Epigenetic Impositions on the Plant Genome: A Paragenetic Function for Chromosomes", Developmental Genetics, Vol. 15, pp. 523-532 (1994).

Richard A. Jorgensen, "Cosuppression, Flower Color Patterns, and Metastable Gene Expression States", Science, Vol. 268, pp. 686-691 (May 1995).

Z.A. Khan et al., "RNA-Directed RNA Polymerases from Healthy and from Virus-Infected Cucumber", Proc. Natl. Acad. Sci. USA, Vol. 83, pp. 2383-2386 (April 1986).

Christian Kunz et al., "Developmentally Regulated Silencing and Reactivation of Tobacco Chitinase Transgene Expression", The Plant Journal, Vol. 10(3), pp. 437-450 (1996).

John A. Lindbo et al., "Induction of a Highly Specific Antiviral State in Transgenic Plants: Implications for Regulation of Gene Expression and Virus Resistance", The Plant Cell, Vol. 5, pp. 1749-1759 (December 1993).

B. Gregory Louis et al., "Purification and Properties of the Ribonucleic Acid-Dependent Ribonucleic Acid Polymerase from *Halobacterium cutirubrum*", Biochem. J., Vol. 128, pp. 755-762 (1972).

Marjori A. Matzke et al., "How and Why Do Plants Inactivate Homologous (Trans)genes?", Plant Physiol., Vol. 107, pp. 679-685 (1995).

Peter Meyer, "Understanding and Controlling Transgene Expression", TIBTECH, Vol. 13, pp. 332-337 (September 1995).

P. Meyer et al., "Homology-Dependent Gene Silencing in Plants", Annu. Rev. Plant Physiol. Plant Mol. Biol., Vol. 47, pp. 23-48 (1996).

M. Prins et al., "RNA-Mediated Virus Resistance in Transgenic Plants", Arch. Virol., Vol. 141, pp. 2259-2276 (1996).

C.P. Romaine et al., "RNA-Dependent RNA Polymerases in Uninfected and Tobacco Mosaic Virus-Infected Tobacco Leaves: Viral-Induced Stimulation of a Host Polymerase Activity", Virology, Vol. 86, pp. 241-253 (1978).

H.L. Sanger et al., "The Possible Links between RNA-Directed DNA Methylation (RdDM), Sense and Antisense RNA, Gene Silencing, Symptom-Induction upon Microbial Infections and RNA-Directed RNA Polymerase (RDRP)", Proceedings from the 8th International Symposium on Molecular Plant-Microbe Interactions Knoxville, Tennessee, pp. 1-8 (July 14-19, 1996).

Winfried Schiebel et al., "RNA-Directed RNA Polymerase from Tomato Leaves: I. Purification and Physical Properties", The Journal of Biological Chemistry, Vol. 263(16), pp. 11851-11857 (1993).

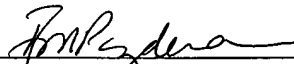
Winfried Schiebel et al., "RNA-Directed RNA Polymerase from Tomato Leaves: II. Catalytic *In Vitro* Properties", The Journal of Biological Chemistry, Vol. 268(16), pp. 11858-11867 (1993).

Titia Sijen et al., "RNA-Mediated Virus Resistance: Role of Repeated Transgenes and Delineation of Targeted Regions", The Plant Cell, Vol. 8, pp. 2277-2294 (December 1996).

- Holly A. Smith et al., "Transgenic Plant Virus Resistance Mediated by Untranslatable Sense RNAs: Expression, Regulation, and Fate of Nonessential RNAs", The Plant Cell, Vol. 6, pp. 1441-1453 (October 1994).
- Maike Stam et al., "The Silence of Genes in Transgenic Plants", Annals of Botany, Vol. 79, pp. 3-12 (1997).
- Maike Stam et al., "Post-Transcriptional Silencing of Chalcone Synthase in *Petunia* by Inverted Transgene Repeats", The Plant Journal, Vol. 12(1), pp. 63-82 (1997).
- Yoichi Takanami et al., "Comparative Studies on Ribonucleic Acid Dependent RNA Polymerases in Cucumber Mosaic Virus Infected Cucumber and Tobacco and Uninfected Tobacco Plants", Biochemistry, Vol. 21, pp. 3161-3167 (1982).
- Crispin B. Taylor, "Comprehending Cosuppression", The Plant Cell, Vol. 9, pp. 1245-1249 (August 1997).
- Helena Van Houdt et al., "Post-Transcriptional Silencing of a Neomycin Phosphotransferase II Transgene Correlates with the Accumulation of Unproductive RNAs and with Increased Cytosine Methylation of 3' Flanking Regions", The Plant Journal, Vol. 12(2), pp. 379-392 (1997).
- Vladimir Volloch et al., "Antisense Globin RNA in Mouse Erythroid Tissues: Structure, Origin, and Possible Function", Proc. Nat. Acad. Sci., Vol. 93, pp. 2476-2481 (March 1996).
- M. Wassenegger, "RNA-directed RNA Polymerase (RdRP) as a Possible Enzyme for *In Vitro* Synthesis of 'Antisense' RNA," 9. Tagung, Molekularbiologie der Pflanzen at Werningerode, Germany (March 5 to March 8, 1996).
- Milton Zaitlin et al., "Plant Virus-Host Interactions", Ann. Rev. Plant Physiol., Vol. 38, pp. 291-315 (1987).
- C. Cogoni et al. "Gene Silencing in *Neurospora crassa* Requires a Protein Homologous to RNA-Dependent RNA Polymerase," Nature 399: 166-169 (1999).
- A. Fire, "RNA-Triggered Gene Silencing," Trends in Genetics 15: 358-363 (1999).
- J.M. Kooter et al. "Listening to the Silent Genes: Transgene Silencing, Gene Regulation and Pathogen Control," Trends in Plant Science 4: 340-347 (1999).
- W. Schiebel et al. "Isolation of an RNA-Directed RNA Polymerase-Specific cDNA Clone from Tomato" The Plant Cell 10: 2087-2101 (1998).

Applicants request that these documents be (1) fully considered by the Examiner during the examination of this application; and (2) printed on any patent that may issue from this application. Applicants also request that a copy of Form PTO-1449, as considered and initialed by the Examiner, be returned with the next communication.

Respectfully submitted,



James F. Halex, Jr. (Reg. No. 27,794)

Attorney for Applicants

Karen E. Brown (Reg. No. 43,866)

R. Minako Pazdera (Reg. No. 46,984)

Agents for Applicants

c/o FISH & NEAVE

1251 Avenue of the Americas

New York, New York 10020-1104

Tel.: (212) 596-9000